

Please substitute the following claim set for the pending claim set.

**IN THE CLAIMS:**

1. (Currently amended) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine ~~the number~~ numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing ~~the~~ a first number which is a sum of numbers of a plurality of individual sequence tags enumerated in the population to ~~the~~ a second number which is a sum of numbers of the plurality of individual sequence tags determined for a genome of a reference cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein a difference ~~in~~ between the first number ~~of the plurality of sequence tags within the window present in the population~~ from and the second number ~~determined for a reference eukaryotic cell~~ indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

2. (original) The method of claim 1 wherein the test eukaryotic cell and the reference eukaryotic cell are of the same species.
3. (original) The method of claim 1 wherein the plurality of sequence tags comprises 10 to 500 contiguous sequence tags.
4. (original) The method of claim 1 wherein the plurality of sequence tags comprises 50 to 1000 contiguous sequence tags.
5. (original) The method of claim 1 wherein the test eukaryotic cell is a human cell.
6. (Original) The method of claim 1 wherein the window spans about 40 kb.
7. (original) The method of claim 1 wherein the window spans about 200 kb.
8. (original) The method of claim 1 wherein the window spans about 600 kb.
9. (original) The method of claim 1 wherein the window spans about 4 Mb.
10. (original) The method of claim 1 wherein less than 50 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
11. (original) The method of claim 1 wherein less than 33 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
12. (original) The method of claim 1 wherein less than 25 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

13. (original) The method of claim 1 wherein less than 20 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
14. (original) The method of claim 1 wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
15. (original) The method of claim 1 wherein the test eukaryotic cell is a cancer cell.
16. (original) The method of claim 1 wherein the test eukaryotic cell is a cell of a person with a hereditary disorder.
17. (original) The method of claim 1 wherein the test eukaryotic cell is a cell of a person with an infectious disease.
18. (original) The method of claim 1 wherein said portions are defined by a first restriction endonuclease cleavage site at a first end of each portion and a second restriction endonuclease cleavage site at a second end of each portion.
19. (original) The method of claim 18 wherein the first restriction endonuclease is *SacI*.
20. (original) The method of claim 18 wherein the second restriction endonuclease is *NlaIII*.
21. (original) The method of claim 18 wherein recognition or cleavage by the first restriction endonuclease is sensitive to DNA methylation.
22. (original) The method of claim 1 wherein said portions are defined by presence of a *BcgI* restriction endonuclease recognition site which is flanked by 12 nucleotides on either end.

23. (original) The method of claim 1 further comprising:

identifying aneuploidy if (a) sequence tags of one or more autosomes are determined to be present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (b) sequence tags of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (c) sequence tags of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.

24. (original) The method of claim 1 wherein the step of enumerating is performed by determining the nucleotide sequence of said sequence tags and recording the number of occurrences of individual sequence tags.

25. (Currently amended) ~~A~~ An isolated population of dimers wherein each dimer comprising comprises two distinct sequence tags from defined portions of a genome of a eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites, wherein each of said sequence tags consists of a fixed number of nucleotides of one of said defined portions of the genome, said fixed number of nucleotides extending from at least one of said restriction endonuclease recognition sites.

26. (Currently amended) The dimer population of claim 25 wherein said portions are defined by a first restriction endonuclease site at a first end of each portion and a second restriction endonuclease site at a second end of each portion.
27. (Currently amended) The dimer population of claim 26 wherein the two sequence tags are joined end-to-end at the ends distal to the second restriction endonuclease site.
28. (Currently amended) The dimer population of claim 26 wherein each dimer further ~~comprising~~ comprises a linker oligonucleotide ligated at each second restriction endonuclease site of the two sequence tags.
29. (Currently amended) The dimer population of claim 25 wherein the eukaryotic cell is a human cell.
30. (Currently amended) A concatamer of dimers made by the process of ligation of dimers in the isolated population according to claim 25.
31. (Currently amended) A concatamer of dimers made by the process of ligation of dimers in the isolated population according to claim 26.
32. (Currently amended) A concatamer of dimers made by the process of ligation of dimers in the isolated population according to claim 27.
33. (Currently amended) A concatamer of dimers made by the process of ligation of dimers in the isolated population according to claim 28.
34. (Currently amended) The dimer population of claim 25 wherein the fixed number of nucleotides is determined by a Type IIS restriction endonuclease used to cleave within said defined portions of the genome.

35. (Currently amended)The dimer population of claim 34 wherein the Type IIS restriction endonuclease is *MmeI*.

36. (Currently amended)The dimer population of claim 35 wherein the fixed number of nucleotides is 20 to 22.

37. (currently amended)A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine ~~the~~ a first number of individual sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of a plurality of sequence tags in the population to ~~the~~ a second number of said plurality of sequence tags calculated to be present in the ~~human~~ genome of the eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein a difference ~~in~~ between the first number ~~of the plurality of sequence tags within the window present in the population from~~ and the second number ~~calculated to be present in the genome of the eukaryotic cell~~ indicates a karyotypic abnormality.

38. (original) The method of claim 37 wherein said portions are defined by a first restriction endonuclease site at a first end of each portion and a second restriction endonuclease site at a second end of each portion.
39. (original) The method of claim 37 wherein said portions are defined by presence of a *BcgI* restriction endonuclease recognition site which is flanked by 12 nucleotides on either end.
40. (original) The method of claim 37 wherein the window comprises 10 to 500 contiguous tags.
41. (original) The method of claim 37 wherein the window comprises 50 to 1000 contiguous tags.
42. (original) The method of claim 37 wherein the test eukaryotic cell is a human cell.
43. (original) The method of claim 37 wherein the window spans about 40 kb.
44. (original) The method of claim 37 wherein the window spans about 200 kb.
45. (original) The method of claim 37 wherein the window spans about 600 kb.
46. (original) The method of claim 37 wherein the window spans about 4 Mb.
47. (original) The method of claim 37 wherein less than 50 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
48. (original) The method of claim 37 wherein less than 33 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.

49. (original) The method of claim 37 wherein less than 25 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
50. (original) The method of claim 37 wherein less than 20 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
51. (original) The method of claim 37 wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
52. (original) The method of claim 37 wherein the test eukaryotic cell is a cancer cell.
53. (original) The method of claim 37 wherein the test eukaryotic cell is a cell of a person with a hereditary disorder.
54. (original) The method of claim 37 wherein the cell is a cell of a person with an infectious disease.
55. (original) The method of claim 38 wherein the first restriction endonuclease is *SacI*.
56. (original) The method of claim 38 wherein the second restriction endonuclease is *NlaIII*.
57. (original) The method of claim 38 wherein recognition or cleavage by the first restriction endonuclease is sensitive to DNA methylation.
58. (original) The method of claim 37 wherein the step of enumerating is performed by determining the nucleotide sequence of said sequence tags and recording the number of occurrences of individual sequence tags.



59. (Currently amended) A method of karyotyping a genome of a test eukaryotic cell,

comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome wherein less than 100 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing ~~the~~ a first number of pieces enumerated within ~~each of the plurality of~~ one of said windows for the test eukaryotic cell to a second number of pieces enumerated within ~~each of the one window plurality of windows~~ for a reference eukaryotic cell, wherein a difference ~~in~~ between the first number of pieces enumerated within a window between the test eukaryotic cell and the second number reference eukaryotic cell indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

60. (Previously presented) The method of claim 59 wherein the test eukaryotic cell and the reference eukaryotic cell are of the same species.

61. (Previously presented) The method of claim 59 wherein the test eukaryotic cell is a human cell.

62. (Currently amended) The method of claim 59 wherein the size of the windows ~~is~~ spans about 40 kb.

63. (Currently amended) The method of claim 59 wherein the size of the windows ~~is~~ spans about 200 kb.

64. (Currently amended)The method of claim 59 wherein the size of the windows ~~is~~ spans about 600 kb.
65. (Currently amended)The method of claim 59 wherein the size of the windows ~~is~~ spans about 4 Mb.
66. (Previously presented)The method of claim 59 wherein less than 50 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
67. (Previously presented)The method of claim 59 wherein less than 33 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
68. (Previously presented)The method of claim 59 wherein less than 25 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
69. (Previously presented)The method of claim 59 wherein less than 20 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
70. (Previously presented)The method of claim 59 wherein less than 15 % of the pieces calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating.
71. (Previously presented) The method of claim 59 wherein the test eukaryotic cell is a cancer cell.
72. (Previously presented) The method of claim 59 wherein the test eukaryotic cell is a cell of a person with a hereditary disorder.
73. (Previously presented) The method of claim 59 wherein the test eukaryotic cell is a cell of a person with an infectious disease.
74. (Previously presented) The method of claim 59 further comprising:  
identifying aneuploidy if (a) pieces of one or more autosomes are determined to be

present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (b) pieces of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (c) pieces of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.

75. (Currently amended) A method of karyotyping a genome of a test eukaryotic cell, comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the a first number of pieces enumerated within one of said ~~each of the plurality of~~ windows for the test eukaryotic cell to a second number of pieces calculated to be present within ~~each of the one window plurality of windows~~ in a human genome of the eukaryotic cell, wherein a difference ~~in between~~ the first number of pieces enumerated within ~~a the~~ window of the test eukaryotic cell and the second number of pieces calculated to be present within the window in ~~a human the eukaryotic cell~~ genome indicates a karyotypic abnormality.

76. (Previously presented) The method of claim 75 wherein the test eukaryotic cell is a human cell.

77. (Currently amended) The method of claim 75 wherein the size of the windows ~~is~~ spans about 40 kb.
78. (Currently amended) The method of claim 75 wherein the size of the windows ~~is~~ spans about 200 kb.
79. (Currently amended) The method of claim 75 wherein the size of the windows ~~is~~ spans about 600 kb.
80. (Currently amended) The method of claim 75 wherein the size of the windows ~~is~~ spans about 4 Mb.
81. (Previously presented) The method of claim 75 wherein the test eukaryotic cell is a cancer cell.
82. (Previously presented) The method of claim 75 wherein the test eukaryotic cell is a cell of a person with a hereditary disorder.
83. (Previously presented) The method of claim 75 wherein the test eukaryotic cell is a cell of a person with an infectious disease.
84. (Previously presented) The method of claim 59 wherein after the step of identifying, the pieces of the genome are matched to precise chromosomal locations on the basis of the nucleotide sequence.
85. (Previously presented) The method of claim 75 wherein after the step of identifying, the pieces of the genome are matched to precise chromosomal locations on the basis of the nucleotide sequence.

86. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of individual sequence tags present in the population;

comparing the first number of a plurality of sequence tags in the population to a second number of the plurality of sequence tags determined for a genome of a reference cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein the plurality of sequence tags comprises 50 to 1000 contiguous sequence tags, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

87. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of individual sequence tags present in the population;

comparing the first number of a plurality of sequence tags in the population to a second number of the plurality of sequence tags determined for a genome of a reference cell, wherein

the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

88. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of individual sequence tags present in the population;

comparing the first number of a plurality of sequence tags in the population to a second number of said plurality of sequence tags calculated to be present in the genome of the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein the plurality of sequence tags comprises 50 to 1000 contiguous sequence tags, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

89. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of individual sequence tags present in the population;

comparing the first number of a plurality of sequence tags in the population to a second number of said plurality of sequence tags calculated to be present in the genome of the eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the species of the eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

90. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome, wherein the window spans about 200 kb;

comparing a first number of pieces enumerated within a plurality of windows for the test eukaryotic cell to a second number of pieces enumerated within the plurality of windows for a reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

91. (New) A method of karyotyping a genome of a test eukaryotic cell, comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome of the test eukaryotic cell, wherein the window spans about 200 kb;

comparing a first number of pieces enumerated within a window for the test eukaryotic cell to a second number of pieces calculated to be present within the window in the genome of the eukaryotic cell, wherein a difference between the first number of pieces enumerated within the window of the test eukaryotic cell and the second number of pieces calculated to be present within the window in the eukaryotic cell genome indicates a karyotypic abnormality.